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REMARKS

In the Office Action mailed June 30, 2004, claims 42 and 44-48 are rejected under 35 USC Section 103(a) as being obvious over US Patent No. 5,770,195 in view of US Patent No. 5,720,954, and Burton *et al. Am J. Vet. Res* 42(20):308-310 (1981).

Applicants respectfully request withdrawal of the rejection in view of the following amendments and remarks. Independent claims 42 and 47 are amended herein to refer to a lower limit for the HER2 antibody concentration of about 80mg/mL as supported on at least page 22, line 29. In addition, claim 48, directed to SQ administration, has been incorporated in claim 47. These amendments further distinguish the presently claimed invention over the cited art.

Claims 42 and 47 of the present application concern subcutaneous administration of a HER2 antibody formulation, where the concentration of the antibody in the formulation is from about 80mg/mL-400mg/mL. Applicants submit that the Examiner's rejection fails to make out a *prima facie* case for obviousness in that neither reference refers to either SQ administration or administration of a high HER2 antibody concentration formulation.

As to SQ administration, the Examiner urges that "there would be a reasonable expectation of success for one of ordinary skill in the art to use subcutaneous administration of an antibody because the optimization of administration routes is clearly within the purview of the skilled artisan." The Examiner further states that the '195 patent refers to optimization of the administration means. The Examiner fails to provide any evidence that SQ administration would constitute optimization of IV administration of a HER2 antibody. Applicants submit that SQ administration would not be considered optimization of IV administration as in the art, especially for cancer therapy where the HER2 antibody needs to get to its target site.

With respect to the 50mg/mL-400mg/mL concentration of the HER2 antibody, the Examiner urges that "a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties." Claims 42 and 47 as amended herein recite that the lower limit for the

antibody concentration is about 80mg/mL. The cited art, on the other hand, refers to an upper limit for the antibody concentration in the formulation of 10mg/mL. Applicants submit that the skilled person would clearly *not* consider "1mg/mL to 10mg/mL" as in the cited art to be "close enough" to "80mg/mL-400mg/mL" such that the formulations in the prior art and the present application would have the same properties. Indeed, the concentration of antibody delivered would be substantially different. Moreover, while high antibody concentrations as presently claimed have decreased stability, *e.g.* due to aggregation, the present application demonstrates how to make a stable high HER2 antibody concentration formulations suitable for SQ administration. Such guidance is not provided by the cited art. Hence, Applicants submit that the pending claims are patentable over the cited art.

Reconsideration and withdrawal of the rejection is respectfully requested in view of the above amendments and remarks.

Respectfully submitted,
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